

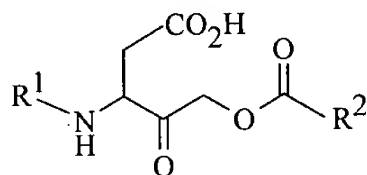


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In The Claims:

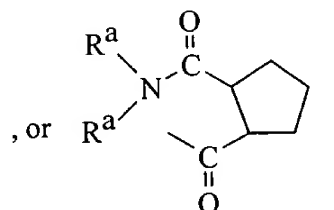
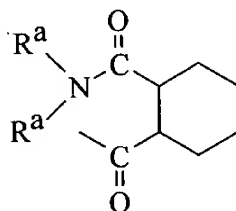
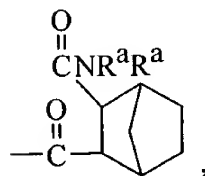
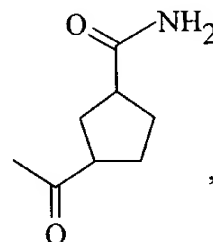
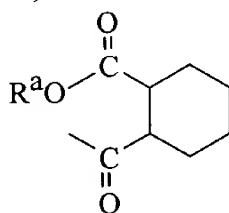
✓
Please amend claims 1 and 52 - 54 as follows:

1. (Amended Four Times) A compound of the Formula I



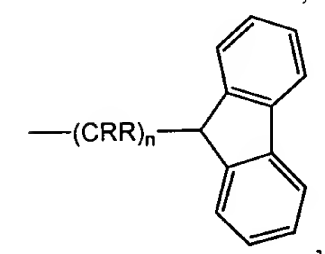
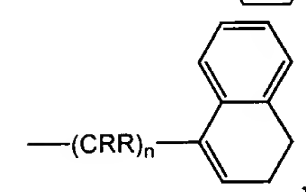
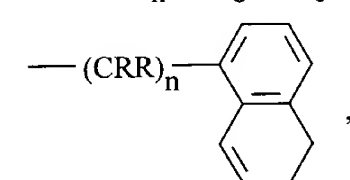
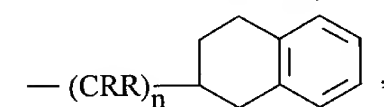
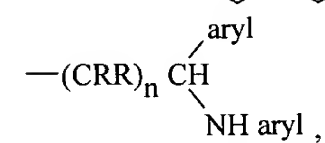
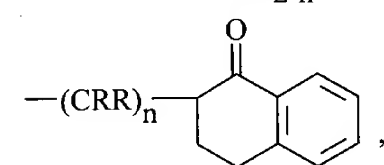
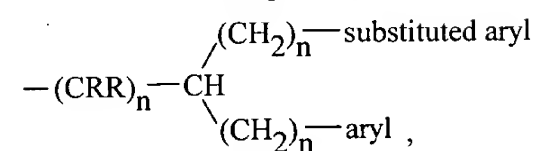
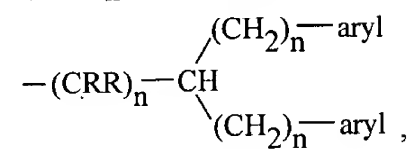
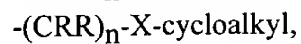
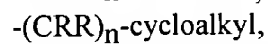
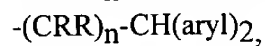
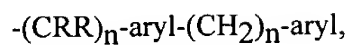
I

wherein R¹ is $\begin{array}{c} \text{O} \\ || \\ \text{R}^3\text{OC}-, \\ \text{R}^3\text{CO}-, \\ \text{R}^3\text{SO}_2-, \\ \text{R}^a \\ | \\ \text{R}^5\text{NCHR}^6\text{CO}-, \end{array}$

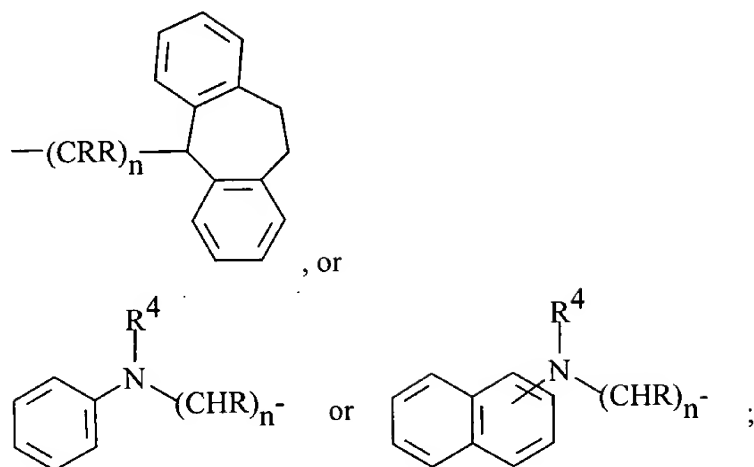


each R^a is independently hydrogen, C₁-C₆ alkyl, or -(CH₂)_n aryl;

R² is -(CRR)_n-aryl,
-(CRR)_n-X-aryl,
-(CRR)_n-(substituted-aryl),
-(CRR)_n-X-(substituted-aryl),
-(CRR)_n-aryl-aryl,



1
D
cont'd



each R is independently hydrogen, C₁-C₆ alkyl, halogen or hydroxy;

X is O or S;

R³ is C₁-C₆ alkyl,

aryl,

-(CHR)_n-aryl,

-(CHR)_n-substituted aryl,

$\begin{array}{c} O \\ || \\ -(CRR)_n COR^a, \end{array}$

-(CRR)_nO(CH₂)_n-aryl,

cycloalkyl,

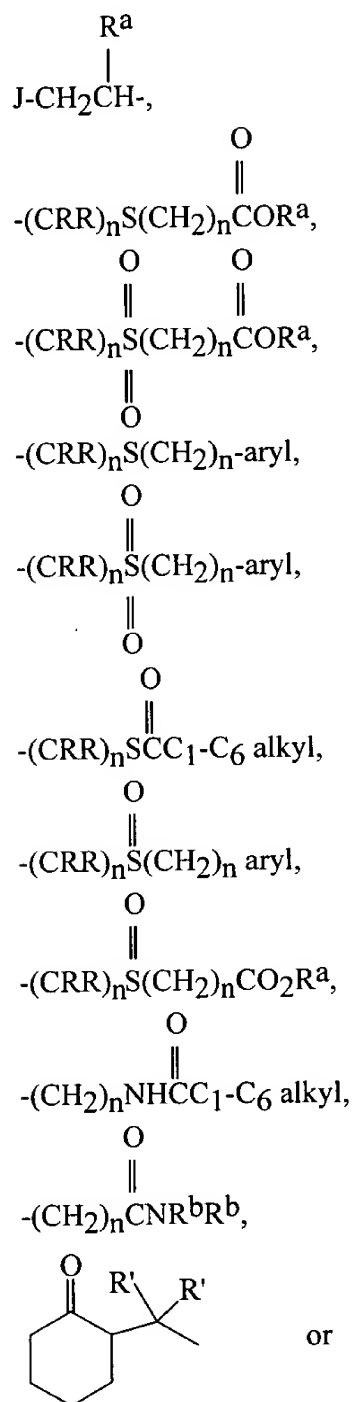
substituted cycloalkyl,

$\begin{array}{c} O \\ || \\ -(CRR)_n CNR^aR^a, \end{array}$

$\begin{array}{c} O \\ || \\ -(CRR)_n -S-(CH_2)_n \text{ aryl}, \end{array}$

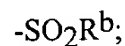
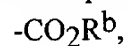
$\begin{array}{c} O \\ || \\ O \\ || \\ -(CRR)_n -SC_1-C_6 \text{ alkyl}, \\ O \end{array}$

1
cont'd



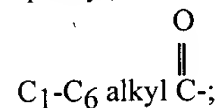
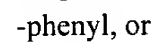
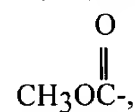
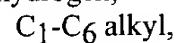
each R' is independently C₁-C₆ alkyl,
 C₁-C₆ alkylaryl,
 aryl, or
 hydrogen;

each J is independently

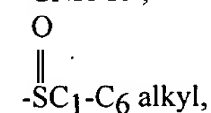
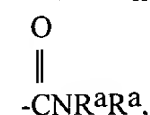
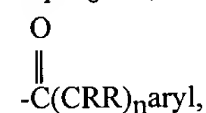
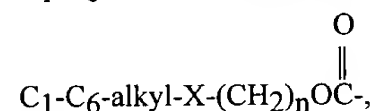
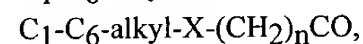
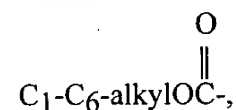
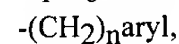


each R^b is independently hydrogen, C_1 - C_6 alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

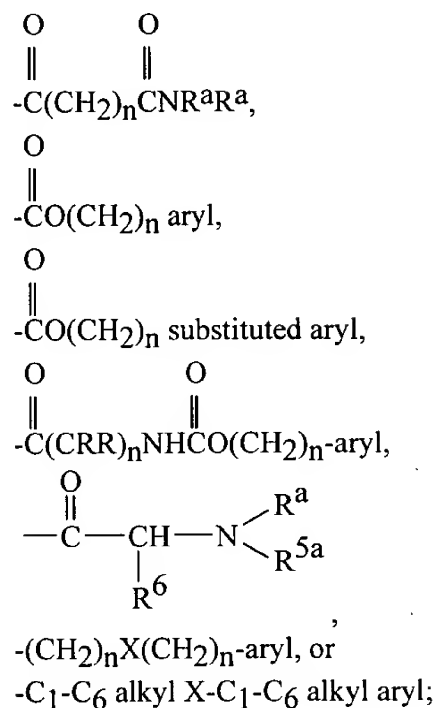
R^4 is hydrogen,



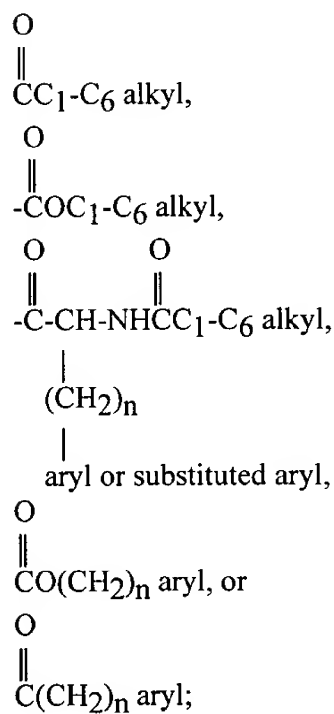
R^5 is C_1 - C_6 alkyl-CO-,



1
Cont'd



R^{5a} is



R⁶ is hydrogen,

C₁-C₆ alkyl, -(CH₂)_n aryl, -(CH₂)_nCO₂R^a, or hydroxyl substituted C₁-C₆ alkyl;

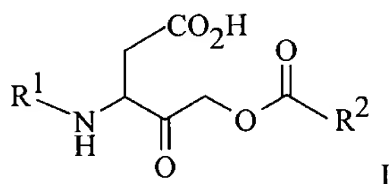
each n is independently 0 to 3, and the pharmaceutically acceptable salts thereof;

excluding the following compounds:

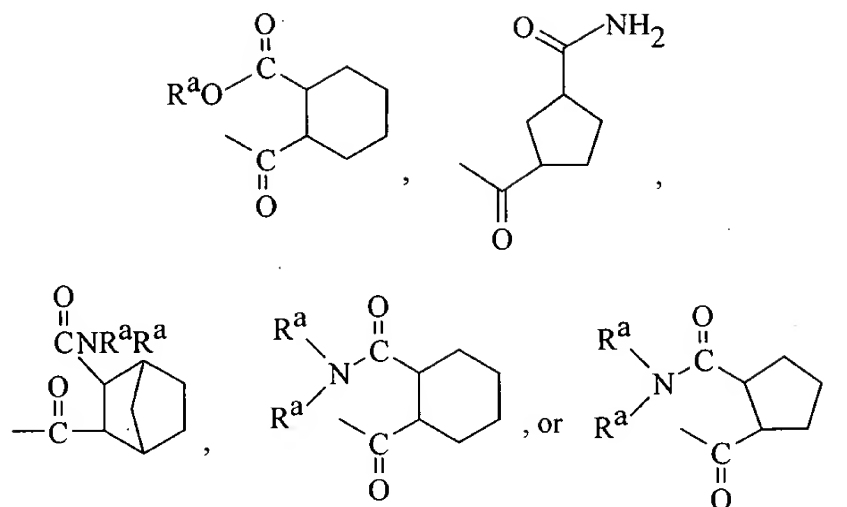
N-(3-Phenylpropionyl)-L-valine-L-alanine-L-aspartic acid 2,6-dihydroxybenzoyloxymethyl ketone;
N-(3-Phenylpropionyl)-L-valine-L-alanine-L-aspartic acid 2,6-dimethylbenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 2,6-ditrifluoromethyl benzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 2,6-dimethoxybenzoyloxy methyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 2,-dichloro-3-(benzyloxy)benzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 2-acetamido-6-chlorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 2,6-difluorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 3-(N-butylsulfonamido)-2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 2,6-dichloro-3-sulfonamido benzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 3-(N-benzylsulfonamido)-2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-aspartic acid 3-(N-(2-aminoacetamidoyl)-sulfonamido)-2,6-dichlorobenzoyloxymethyl ketone;
N-Methoxycarbonyl-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Methoxycarbonyl glycine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Methoxycarbonyl-L-phenylalanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Methoxycarbonyl-L-valine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-valine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-L-valine-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-(3-Phenylpropionyl)-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Methoxycarbonyl-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-(4-N,N-dimethylaminomethyl)benzoyl-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxycarbonyl-D-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Methoxy-glycine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Methoxy-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Methoxy-L-valine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxy-L-valine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxy-D-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxy-L-alanine-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxy-L-valine-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
N-Benzyloxy-D-alanine-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;

N-(N-phenylpropionyl-valinyl-alaninyl)-3-amino-4-oxo-5-(2,6-bistrifluoromethylbenzoyloxy) pentanoic acid;
 N-(N-phenylpropionyl-valinyl-alaninyl)-3-amino-4-oxo-5-benzoyloxy pentanoic acid;
 N-(N-Acetyl-tyrosinyl-valinyl-alaninyl)-3-amino-4-oxo-5-(pentafluorobenzoyloxy) pentanoic acid;
 3-Phenylpropionyl-L-valine-L-alanine-aspartic acid 2-phenylethylcarbonyloxymethyl ketone;
 Adamantane-1-carboxylic acid 3-[2-(2-benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-4-carboxy-2-oxo-butyl ester;
 3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-5-diphenylacetoxo-4-oxo-pentanoic acid;
 2,6-Dichloro-benzoic acid 3-(5-benzyloxycarbonylamino-naphthalene-1-sulfonylamino)-4-carboxy-2-oxo-butyl ester;
 2,6-Dichloro-benzoic acid 3-[2-(3-benzyloxycarbonylamino-phenyl)-propionylamino]-4-carboxy-2-oxo-butyl ester;
 2,6-Dichloro-benzoic acid 3-[2-(6-benzyloxycarbonyloxy-naphthalen-2-yl)-propionylamino]-4-carboxy-2-oxo-butyl ester;
 2,6-Dichloro-benzoic acid 3-(5-benzyloxycarbonylamino-naphthalene-1-sulfonylamino)-4-carboxy-2-oxo-butyl ester;
 2,6-Dichloro-benzoic acid 3-[(5-benzyloxycarbonylamino-naphthalene-1-carbonyl)-amino]-4-carboxy-2-oxo-butyl ester; and
 2,6-Dichloro-benzoic acid 3-[(4-benzyloxycarbonylamino-cyclohexanecarbonyl)-amino]-4-carboxy-2-oxo-butyl ester.

52. (Amended) A compound of the Formula I

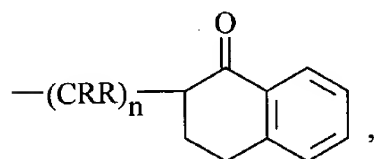
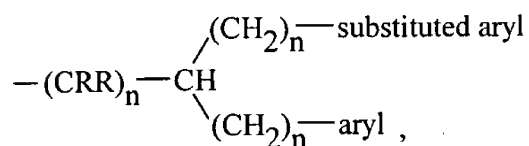
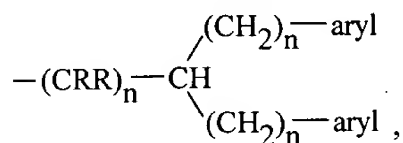


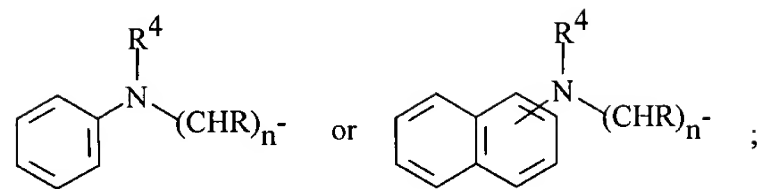
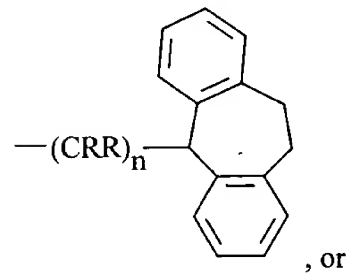
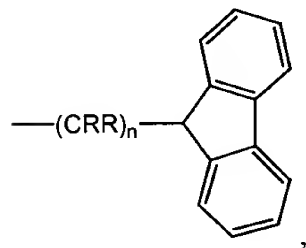
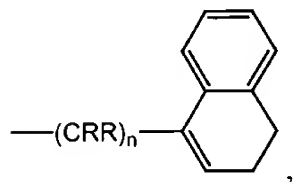
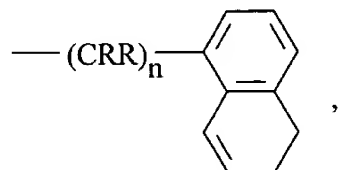
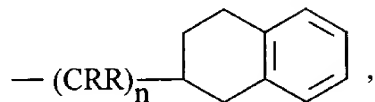
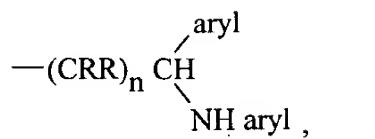
wherein R¹ is $\text{R}^3\text{OC}-$,
 $\text{R}^3\text{CO}-$,
 R^3SO_2- ,
 $\begin{array}{c} \text{R}^a \\ | \\ \text{R}^5\text{NCHR}^6\text{CO}- \end{array}$



each R^a is independently hydrogen, C_1 - C_6 alkyl, or $-(CH_2)_n$ aryl;

R^2 is $-(CRR)_n$ -aryl,
 $-(CRR)_n$ -X-aryl,
 $-(CRR)_n$ -(substituted-aryl), provided that the aryl group is not substituted with
 alkoxy, halogen, or trifluoromethyl,
 $-(CRR)_n$ -X-(substituted-aryl),
 $-(CRR)_n$ -aryl-aryl,
 $-(CRR)_n$ -aryl- $(CH_2)_n$ -aryl,
 $-(CRR)_n$ -CH(aryl) $_2$,
 $-(CRR)_n$ -cycloalkyl,
 $-(CRR)_n$ -X-cycloalkyl,





each R is independently hydrogen, C₁-C₆ alkyl, halogen or hydroxy;

X is O or S;

R³ is C₁-C₆ alkyl,
 aryl,

-(CHR)_n-aryl,
 -(CHR)_n-substituted aryl,

$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{COR}^a, \\ \text{-(CRR)}_n\text{O(CH}_2)_n\text{-aryl,} \\ \text{cycloalkyl,} \\ \text{substituted cycloalkyl,} \end{array}$

$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{CNR}^a\text{R}^a, \end{array}$

$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{-S-(CH}_2)_n\text{ aryl,} \end{array}$

$\begin{array}{c} \text{O} \\ || \\ \text{O} \\ || \\ \text{-(CRR)}_n\text{-SC}_1\text{-C}_6\text{ alkyl,} \\ \text{O} \end{array}$

$\begin{array}{c} \text{R}^a \\ | \\ \text{J-CH}_2\text{CH-,} \end{array}$

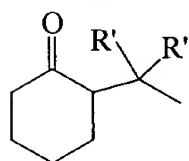
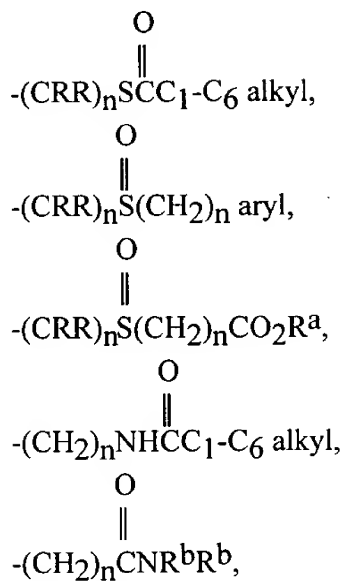
$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{S(CH}_2)_n\text{COR}^a, \end{array}$

$\begin{array}{c} \text{O} \quad \text{O} \\ || \quad || \\ \text{-(CRR)}_n\text{S(CH}_2)_n\text{COR}^a, \end{array}$

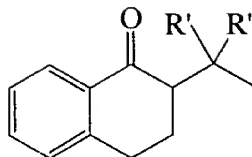
$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{S(CH}_2)_n\text{-aryl,} \end{array}$

$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{S(CH}_2)_n\text{-aryl,} \\ \text{O} \end{array}$

2
 1
 contd



or

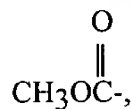


each R' is independently C₁-C₆ alkyl,
 C₁-C₆ alkylaryl,
 aryl, or
 hydrogen;

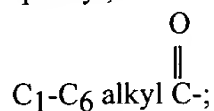
each J is independently
 -CO₂R^b,
 -CONR^bR^b,
 -SO₂NR^bR^b, or
 -SO₂R^b;

each R^b is independently hydrogen, C₁-C₆ alkyl, aryl, substituted aryl, arylalkyl, or
 substituted arylalkyl;

R⁴ is hydrogen,
 C₁-C₆ alkyl,

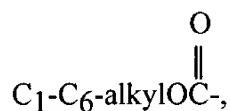


-phenyl, or

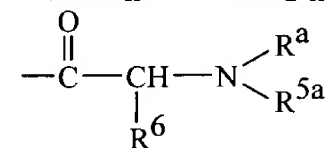
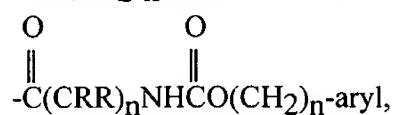
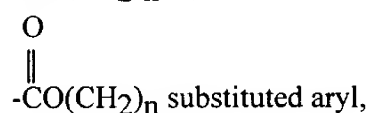
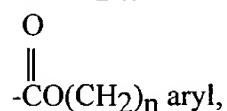
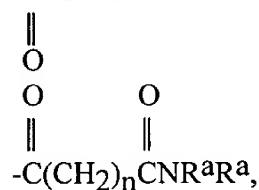
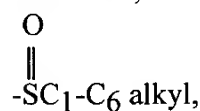
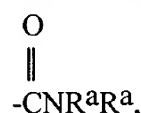
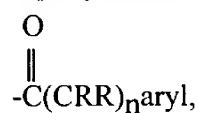
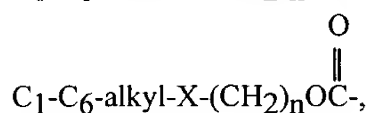


R⁵ is C₁-C₆ alkyl-CO-,

-(CH₂)_n aryl,



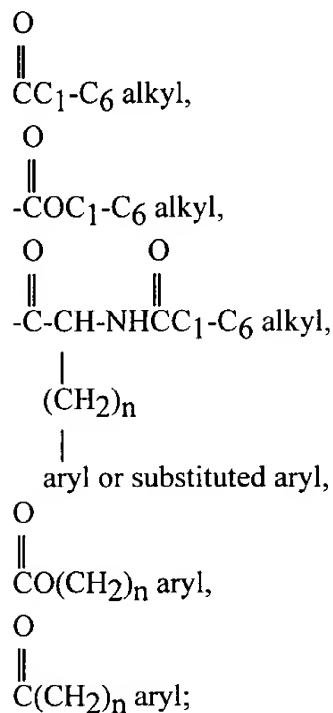
C₁-C₆-alkyl-X-(CH₂)_nCO,



-(CH₂)_nX(CH₂)_n-aryl, or

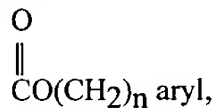
-C₁-C₆ alkyl X-C₁-C₆ alkyl aryl;

R^{5a} is



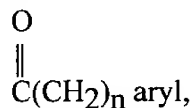
R⁶ is hydrogen, C₁-C₆ alkyl, -(CH₂)_n aryl, -(CH₂)_nCO₂R^a, or hydroxyl substituted C₁-C₆ alkyl;

each n is independently 0 to 3,
provided that when R^{5a} is



then n is 0, 2, or 3, and

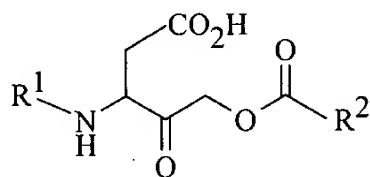
provided that when R^{5a} is



then n is 0, 1, or 3,

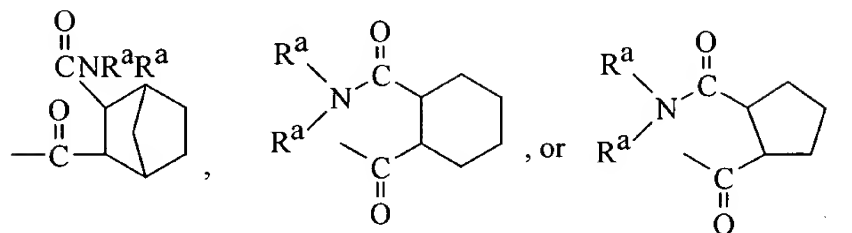
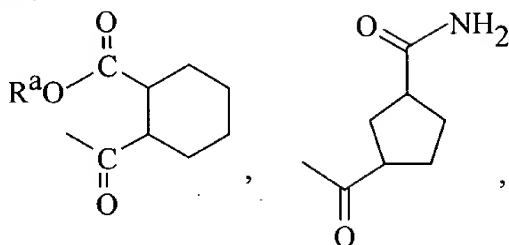
and the pharmaceutically acceptable salts thereof.

53. (Amended) A compound of the Formula I



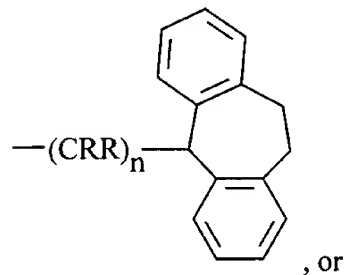
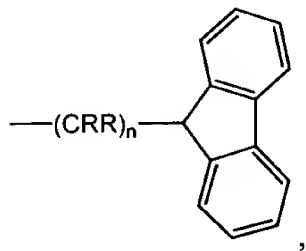
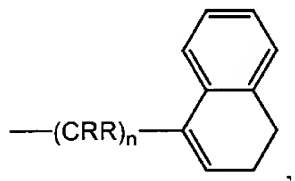
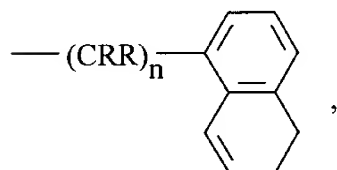
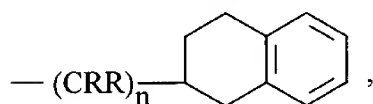
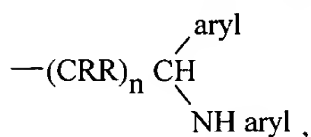
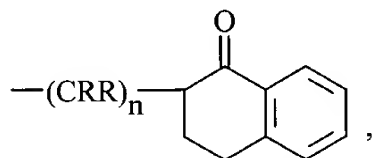
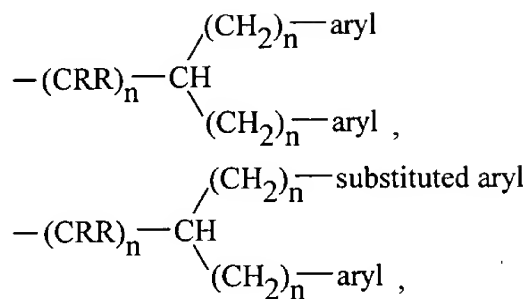
I

wherein R¹ is $\text{R}^3\text{OC}-$,
 $\text{R}^3\text{CO}-$,
 R^3SO_2- ,
 R^a
 $\text{R}^5\text{NCHR}^6\text{CO}-$,

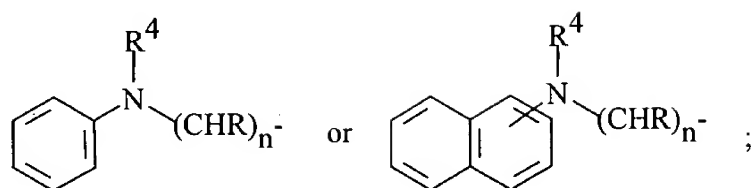


each R^a is independently hydrogen, C₁-C₆ alkyl, or -(CH₂)_n aryl;

R² is -(CRR)_n-aryl,
 -(CRR)_n-X-aryl,
 -(CRR)_n-X-(substituted-aryl),
 -(CRR)_n-aryl-aryl,
 -(CRR)_n-aryl-(CH₂)_n-aryl,
 -(CRR)_n-CH(aryl)₂,
 -(CRR)_n-cycloalkyl,
 -(CRR)_n-X-cycloalkyl,



12
contd



each R is independently hydrogen, C₁-C₆ alkyl, halogen or hydroxy;

X is O or S;

R³ is C₁-C₆ alkyl,
 aryl,
 -(CHR)_n-aryl,
 -(CHR)_n-substituted aryl,

$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{COR}^a, \\ \text{-(CRR)}_n\text{O}(\text{CH}_2)_n\text{-aryl,} \\ \text{cycloalkyl,} \\ \text{substituted cycloalkyl,} \end{array}$

$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{CNR}^a\text{R}^a, \end{array}$

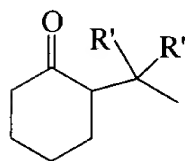
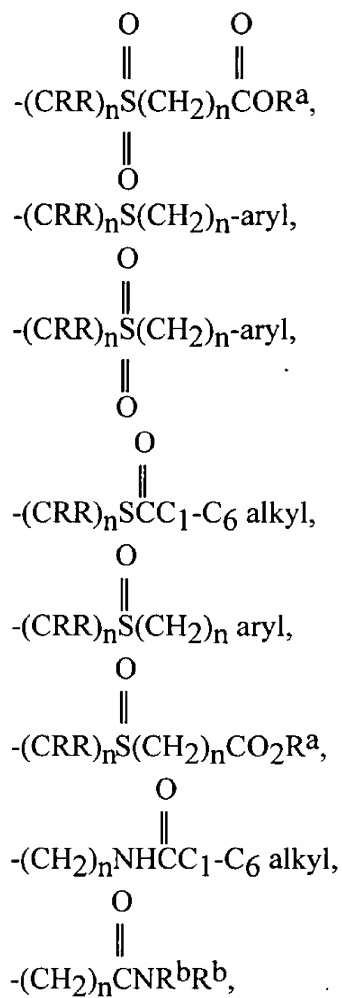
$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{-S-(CH}_2)_n\text{ aryl,} \end{array}$

$\begin{array}{c} \text{O} \\ || \\ \text{O} \\ || \\ \text{-(CRR)}_n\text{-SC}_1\text{-C}_6\text{ alkyl,} \\ \text{O} \end{array}$

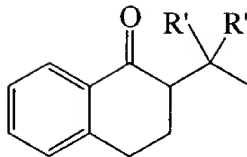
$\begin{array}{c} \text{R}^a \\ | \\ \text{J-CH}_2\text{CH-,} \end{array}$

$\begin{array}{c} \text{O} \\ || \\ \text{-(CRR)}_n\text{S(CH}_2)_n\text{COR}^a, \end{array}$

①²
 contd



or



each R' is independently C₁-C₆ alkyl,
 C₁-C₆ alkylaryl,
 aryl, or
 hydrogen;

each J is independently
 -CO₂R^b,
 -CONR^bR^b,
 -SO₂NR^bR^b, or
 -SO₂R^b;

each R^b is independently hydrogen, C_1 - C_6 alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

R^4 is hydrogen,

C_1 - C_6 alkyl,

$\begin{array}{c} O \\ || \\ CH_3OC-, \end{array}$

-phenyl, or

$\begin{array}{c} O \\ || \\ C_1-C_6 \text{ alkyl } C-, \end{array}$

R^5 is C_1 - C_6 alkyl-CO-,

-(CH_2) $_n$ aryl,

$\begin{array}{c} O \\ || \\ C_1-C_6\text{-alkyl}OC-, \end{array}$

C_1 - C_6 -alkyl-X-(CH_2) $_n$ CO,

$\begin{array}{c} O \\ || \\ C_1-C_6\text{-alkyl-X-(CH}_2\text{)}_nOC-, \end{array}$

$\begin{array}{c} O \\ || \\ -C(CRR)_n\text{aryl,} \end{array}$

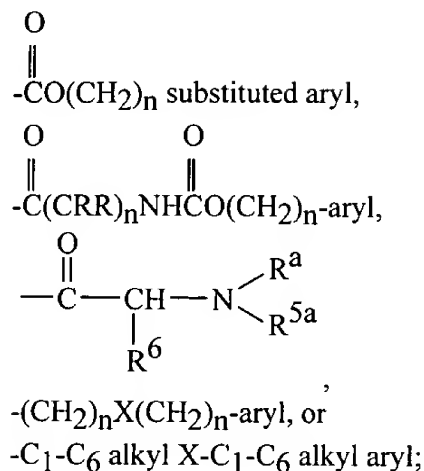
$\begin{array}{c} O \\ || \\ -CNR^aR^a, \end{array}$

$\begin{array}{c} O \\ || \\ -SC_1-C_6 \text{ alkyl,} \end{array}$

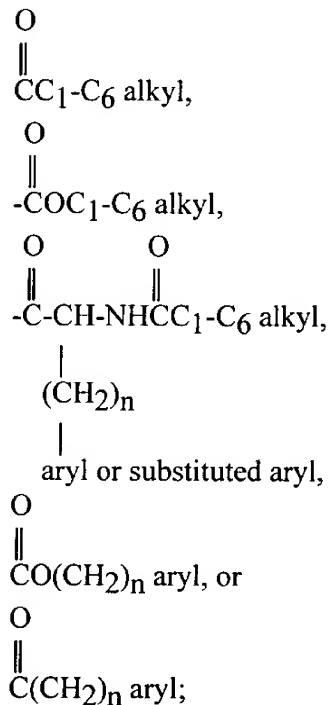
$\begin{array}{c} O \\ || \\ O \quad O \\ || \quad || \\ -C(CH_2)_n\text{CNR}^aR^a, \end{array}$

$\begin{array}{c} O \\ || \\ -CO(CH_2)_n \text{ aryl,} \end{array}$

①²
 cont'd

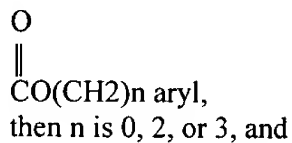


R^{5a} is



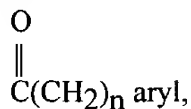
R⁶ is hydrogen, C₁-C₆ alkyl, $-(\text{CH}_2)_n$ aryl, $-(\text{CH}_2)_n\text{CO}_2\text{R}^a$, or hydroxyl substituted C₁-C₆ alkyl;

each n is independently 0 to 3,
 provided that when R^{5a} is



12
 cont'd

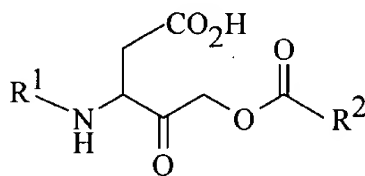
provided that when R^{5a} is



then n is 0, 1, or 3,

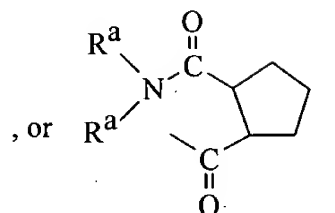
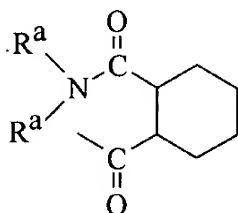
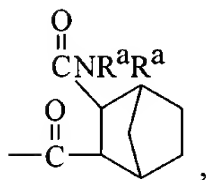
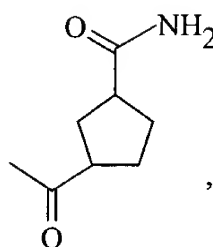
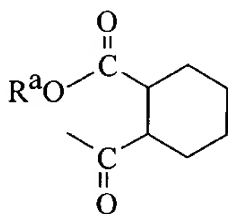
and the pharmaceutically acceptable salts thereof.

54. (Amended) A compound of the Formula I



I

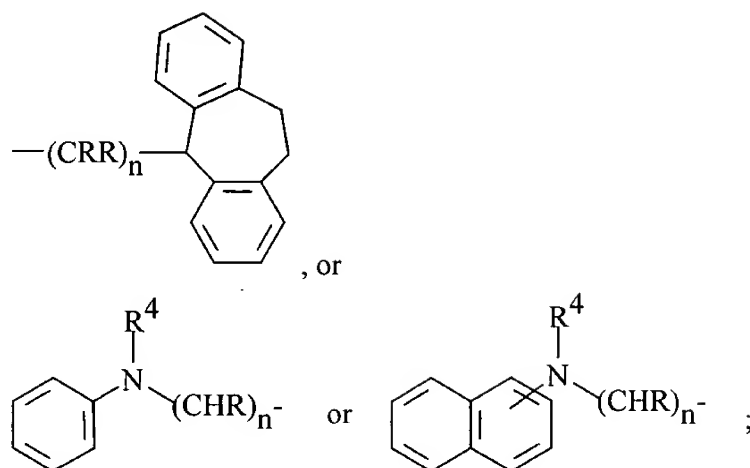
wherein R¹ is $\begin{array}{c} \text{O} \\ \parallel \\ \text{R}^3\text{OC}-, \\ \text{R}^3\text{CO}-, \\ \text{R}^3\text{SO}_2-, \\ \text{R}^a \\ | \\ \text{R}^5\text{NCHR}^6\text{CO}-, \end{array}$



each R^a is independently hydrogen, C₁-C₆ alkyl, or -(CH₂)_n aryl;

R² is -(CRR)_n-aryl,

D²
cont'd



each R is independently hydrogen, C₁-C₆ alkyl, halogen or hydroxy;

X is O or S;

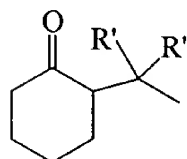
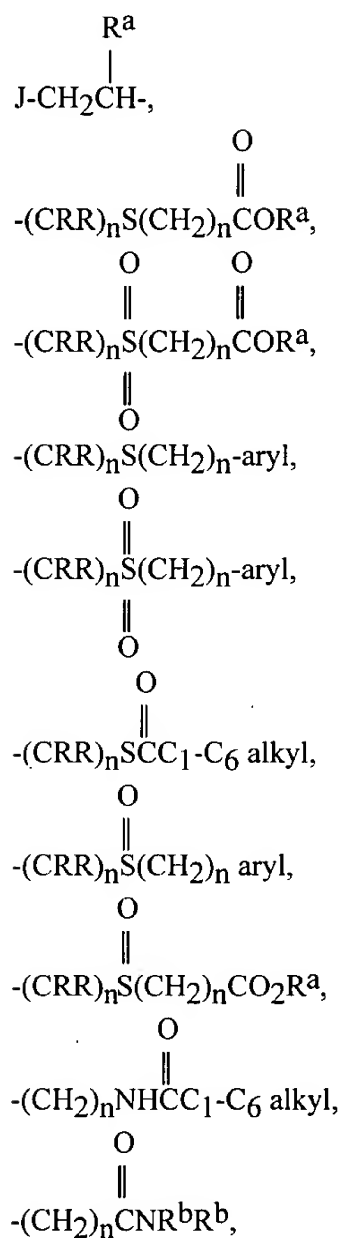
R³ is C₁-C₆ alkyl,
 aryl,
 -(CHR)_n-aryl,
 -(CHR)_n-substituted aryl,

O
 \parallel
 -(CRR)_nCOR^a,
 -(CRR)_nO(CH₂)_n-aryl,
 cycloalkyl,
 substituted cycloalkyl,

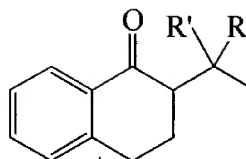
O
 \parallel
 -(CRR)_nCNR^aR^a,
 O
 \parallel
 -(CRR)_n-S-(CH₂)_n-aryl,

O
 \parallel
 O
 \parallel
 -(CRR)_n-SC₁-C₆ alkyl,
 O
 \parallel

12
 contd



or



each R' is independently C₁-C₆ alkyl,
 C₁-C₆ alkylaryl,
 aryl, or
 hydrogen;

each J is independently

-CO₂R^b,
 -CONR^bR^b,
 -SO₂NR^bR^b, or
 -SO₂R^b;

each R^b is independently hydrogen, C₁-C₆ alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

R⁴ is hydrogen,

C₁-C₆ alkyl,

$\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3\text{OC}- \end{array}$,

-phenyl, or

$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}_1\text{-C}_6 \text{ alkyl C}- \end{array}$;

R⁵ is C₁-C₆ alkyl-CO-,

-(CH₂)_n aryl,

$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}_1\text{-C}_6\text{-alkylOC}- \end{array}$,

C₁-C₆-alkyl-X-(CH₂)_nCO,

$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}_1\text{-C}_6\text{-alkyl-X-(CH}_2\text{)}_n\text{OC}- \end{array}$,

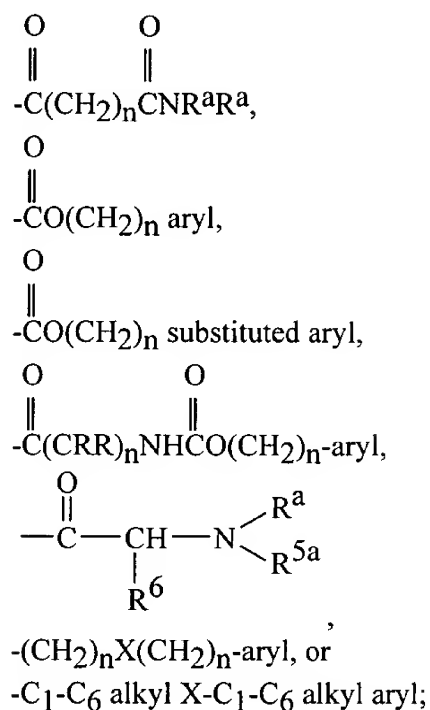
$\begin{array}{c} \text{O} \\ \parallel \\ \text{-C(CRR)}_n\text{aryl,} \end{array}$

$\begin{array}{c} \text{O} \\ \parallel \\ \text{-CNR}^a\text{R}^a, \end{array}$

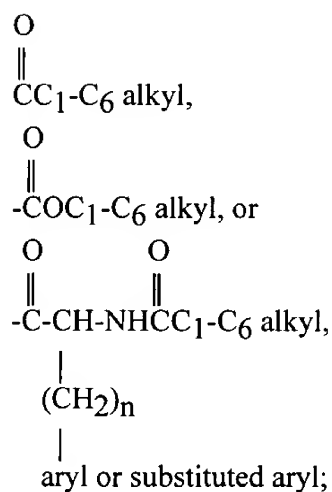
$\begin{array}{c} \text{O} \\ \parallel \\ \text{-SC}_1\text{-C}_6 \text{ alkyl,} \end{array}$

$\begin{array}{c} \text{O} \\ \parallel \end{array}$

①²
 cont'd



R^{5a} is



R⁶ is hydrogen, C₁-C₆ alkyl, -(CH₂)_n aryl, -(CH₂)_nCO₂R^a, or hydroxyl substituted C₁-C₆ alkyl;

each n is independently 0 to 3, and the pharmaceutically acceptable salts thereof.

Please add new claims 55 - 61 as follows:

- D³
55. (New) A pharmaceutically acceptable ester, amide, or prodrug of a compound of formula I according to Claim 1, wherein said ester is a C₅-C₇ cycloalkyl ester or an arylalkyl ester.
 56. (New) The pharmaceutically acceptable ester of a compound of formula I according to Claim 55.
 57. (New) The pharmaceutically acceptable amide of a compound of formula I according to Claim 55.
 58. (New) The pharmaceutically acceptable prodrug of a compound of formula I according to Claim 55.
 59. (New) The pharmaceutically acceptable amide of a compound of formula I according to Claim 57, wherein said amide is derived from ammonia, primary C₁-C₆ alkyl amines, and secondary C₁-C₆ dialkyl amines; wherein the alkyl groups are straight or branched chain.
 60. (New) The pharmaceutically acceptable amide of a compound of formula I according to Claim 57, wherein said amide is derived from ammonia, primary C₁-C₃ alkyl amines, and secondary C₁-C₂ dialkyl amines; wherein the alkyl groups are straight or branched chain.
 61. (New) The pharmaceutically acceptable prodrug of a compound of formula I according to Claim 55.